

IN THE CLAIMS:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims

This listing of claims replaces all prior versions, and listings, of claims in the application:

1-34. (Canceled)

35. (Currently Amended) A method of treating a subject having a cell proliferative disorder, the method comprising:

a) contacting the subject with a therapeutically effective amount of a replication competent retrovirus comprising:

a nucleic acid sequence encoding a retroviral GAG protein;

a nucleic acid sequence encoding a retroviral POL protein;

a nucleic acid sequence encoding a retroviral envelope;

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' or 3' or 5' and 3' end of the oncoretroviral polynucleotide sequence;

a cassette comprising an internal ribosome entry site (IRES) operably linked to a heterologous nucleic acid sequence encoding a polypeptide that converts a nontoxic prodrug to a toxic drug, wherein the cassette is positioned 5' to the 3' LTR

sequence and/or 3' to the sequence encoding the retroviral envelope and ~~5' to the 3' LTR sequence~~; and

cis-acting sequences for reverse transcription, packaging and integration in a target cell;

b) contacting the subject with a nontoxic prodrug that is converted ~~in to~~ into a toxic drug by the polypeptide.

36. (Currently Amended) The method of ~~claim 1~~ claim 35, wherein the cell proliferative disorder is selected from the group consisting of lung cancer, colon-rectum cancer, brain cancer, breast cancer, prostate cancer, urinary tract cancer, uterine cancer lymphoma, oral cancer, pancreatic cancer, leukemia, melanoma, stomach cancer and ovarian cancer.

37. (Previously Presented) The method of claim 36, wherein the brain cancer is glioblastoma multiforme.

38. (Previously Presented) The method of claim 35, wherein the Long Terminal repeat (LTR) sequences further comprise a tissue-specific promoter sequence that permits replication of the retrovirus in a targeted tissue.

39. (Currently Amended) The method of ~~claim 36~~ claim 38, wherein the tissue-specific promoter sequence comprises at least one androgen response element (ARE).

40. (Currently Amended) The method of ~~claim 37~~ claim 39, wherein the androgen response element (ARE) tissue-specific

promoter sequence is ~~derived~~ obtained from the probasin promoter.

41. (Currently Amended) The method of ~~claim 1~~ claim 38, wherein the tissue-specific promoter sequence comprises nucleotides -426 to +28 of the rat probasin gene.

42. (Previously Presented) The retrovirus of claim 35, wherein the polypeptide that converts a nontoxic prodrug in to a toxic drug is thymidine kinase or purine nucleoside phosphorylase (PNP).

43. (Previously Presented) The method of claim 35, wherein the retroviral envelope comprises a chimeric ENV protein, wherein the chimeric ENV protein comprises a targeting ligand that specifically targets the retrovirus to a specific tissue.

44. (Previously Presented) The method of claim 43, wherein the targeting ligand is an antibody, a receptor, or a receptor ligand.

45. (Previously Presented) The method of claim 35, wherein the subject is a mammal.

46. (Previously Presented) The method of claim 45, wherein the mammal is a human.

47. (Previously Presented) The method of claim 35, wherein the contacting is by in vivo administration of the retrovirus.

48. (Previously Presented) The method of claim 47, wherein the in vivo administration is by systemic, local, or topical administration.

49. (Previously Presented) The method of claim 35, wherein the oncoretroviral polynucleotide sequence is selected from the group consisting of murine leukemia virus (MLV), Moloney murine leukemia virus (MoMLV), Gibbon ape leukemia virus (GALV) and Human Foamy Virus (HFV).

50. (Previously Presented) The method of claim 49, wherein the MLV is an amphotropic MLV.

51. (Currently Amended) The method of claim 35, wherein the ~~retroviral vector~~ retroviral competent retrovirus is contained in a pharmaceutically acceptable carrier.

52. (Currently Amended) A method of treating a subject having a cell proliferative disorder, the method comprising:

a) contacting the subject with a therapeutically effective amount of a replication competent retrovirus comprising:

a nucleic acid sequence encoding a retroviral GAG protein;
a nucleic acid sequence encoding a retroviral POL protein;
a nucleic acid sequence encoding a retroviral envelope;

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the retroviral genome, wherein a tissue-specific promoter sequence is contained within the LTR sequences at the 5' or 3' or 5' and 3' end of the oncoretroviral polynucleotide sequence, wherein the tissue specific promoter sequence comprises at least one androgen responsive region ~~derived~~ obtained from the probasin promoter;

a cassette comprising an internal ribosome entry site (IRES) operably linked to a heterologous nucleic acid sequence encoding a polypeptide that converts a nontoxic prodrug to a toxic drug, wherein the cassette is positioned 3' to the sequence encoding the retroviral envelope and 5' to the 3' LTR sequence; and

cis-acting nucleic acid sequences for reverse transcription, packaging and integration in a target cell; and

b) contacting the subject with a nontoxic prodrug that is converted ~~in to~~ into a toxic drug by the polypeptide.

53. (Currently Amended) A method of treating a subject having a cell proliferative disorder, the method comprising:

a) contacting the subject with a therapeutically effective amount of a replication competent retrovirus comprising:

a nucleic acid sequence encoding a retroviral GAG protein;
a nucleic acid sequence encoding a retroviral POL protein;
a nucleic acid sequence encoding a retroviral envelope
comprising a chimeric env protein comprising a targeting ligand;

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the retroviral genome, wherein a tissue-specific promoter sequence is contained within the LTR sequences at the 5' or 3' or 5' and 3' end of the oncoretroviral polynucleotide sequence, wherein the tissue specific promoter sequence comprises at least one androgen responsive region ~~derived~~ obtained from the probasin promoter;

a cassette comprising an internal ribosome entry site (IRES) operably linked to a heterologous nucleic acid sequence encoding a polypeptide that converts a nontoxic prodrug to a toxic drug, wherein the cassette is positioned 3' to the sequence encoding the retroviral envelope and 5' to the 3' LTR sequence; and

cis-acting nucleic acid sequences for reverse transcription, packaging and integration in a target cell; and

b) contacting the subject with a nontoxic prodrug that is converted ~~in-to~~ into a toxic drug by the polypeptide.

54. (Currently Amended) A method of treating a subject having a cell proliferative disorder, the method comprising:

a) contacting the subject with a therapeutically effective amount of a replication competent retrovirus comprising:

- a retroviral GAG protein;
- a retroviral POL protein;
- a retroviral envelope;

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' or 3' or 5' and 3' end of the oncoretroviral polynucleotide sequence;

a cassette comprising an internal ribosome entry site (IRES) operably linked to a heterologous nucleic acid sequence encoding a polypeptide that converts a nontoxic prodrug to a toxic drug, wherein the cassette is positioned 5' to the 3' LTR sequence and/or 3' to the sequence encoding the retroviral envelope ~~and 5' to the 3' LTR sequence~~; and

cis-acting sequences for reverse transcription, packaging and integration in a target cell;

b) contacting the subject with a nontoxic prodrug that is converted ~~in to~~ into a toxic drug by the polypeptide.

--55. (New) A method of treating a subject having a cell proliferative disorder, the method comprising:

(a) contacting the subject with a therapeutically effective amount of a replication competent retrovirus comprising:

an oncoretroviral polynucleotide sequence comprising cis acting sequences for reverse transcription, packaging and integration and Long-Terminal Repeat (LTR) sequences at the 5' and/or 3' end of the oncoretroviral polynucleotide sequence;

a cassette comprising a retroviral GAG protein, a retroviral POL protein and a retroviral envelope protein within the retroviral body;

a cassette comprising an internal ribosome entry site (IRES) operably linked to a heterologous nucleic acid encoding a polypeptide that converts a nontoxic prodrug to a toxic drug,

wherein the cassette is positioned 5' to the 3' LTR and/or 3' to the sequence encoding the retroviral envelope; and

(b) contacting the subject with a nontoxic prodrug that is converted into a toxic drug by the polypeptide encoded by said heterologous nucleic acid.--